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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,420	08/15/2006	Tsukao Yokoyama	YPO1.001APC	9866

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
12/09/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/589,420	YOKOYAMA ET AL.	
	Examiner	Art Unit	
	JAMES L. GRUN	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-21 and 23-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-21 and 23-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The amendment filed 19 August 2009 is acknowledged and has been entered. Claims 32 and 33 are newly added. Claims 1-17 and 22 have been cancelled. Claims 18-21 and 23-33 remain in the case.

Applicant's prior showing of the current ready commercial availability of the "NC1" antibody was sufficient to overcome a prior deposit requirement made in a previous Office action. Applicant is cautioned that the material required for practice of the method may cease to be known and readily available to the public at some future time. Public access during the term of a patent may affect the enforceability of that patent.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-21 and 23-33 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 18 and claims dependent thereupon, the acronym "GBM" should not be used until fully defined at its first occurrence.

In claim 21 and claims dependent thereupon, the acronym "GBM" should not be used until fully defined at its first occurrence.

In claim 32, the relationship of the sample to configure antibody affinity to that obtained from the mammal is not clear, that is it is entirely unclear if affinity is configured with regard to a kidney tissue sample or to some other undefined nephritis sample.

In claim 33, "the following . . . procedure" lacks antecedent basis. The claim is unclear because there is no nexus between the claim clauses; therefore it is entirely unclear if selecting is with regard to binding to a kidney tissue sample or to some other undefined nephritis sample.

Applicant's arguments filed 19 August 2009 have been fully considered but they are not deemed to be persuasive.

Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 21, 23, 24, and 26-31 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Yokoyama et al. (Cell 35: 40, 2003), further in view of Campbell, Cosmo Bio Co. Ltd., Sugihara et al. (J. Pathol. 178: 352, 1996), and Johansson et al. (J. Biol. Chem. 267: 24533,

1992) for reasons of record in the prior rejection of the similar subject matter of these claims. In addition to the reasons of record, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art, e.g. to use the Mono 12D anti-NC1 monoclonal antibody (i.e. "K35MONO" in view of Cosmo Bio Co. Ltd. and applicant's specification at page 12) for antigen detection, cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Claims 18-20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Yokoyama et al. (Cell 35: 40, 2003) together with Cosmo Bio Co. Ltd., Oftshun et al. (US 5871649), Sugihara et al. (J. Pathol. 178: 352, 1996), and applicant's specification at page 12 for reasons similar to those of record in the prior rejection of the similar subject matter of these claims.

The teachings of Yokoyama et al. are as set forth previously and differ from the invention as instantly claimed in not teaching a specific apparatus for use in dialysis removal of NC1 antigen and anti-NC1 antibodies. As set forth, in addition to teaching enzyme-linked immunosorbent immunoassays for the detection of circulating noncollagenous domain of collagen (NC1) antigen and antibodies specific for NC1 antigen in biological samples from patients with and without nephritis Yokoyama et al. teach that an improvement of dialysis therapy would involve the removal of NC1 antigen and antibodies specific for NC1 antigen from the glomerulonephritis patient during dialysis (see e.g. translation pages 7 and 8).

The Cosmo Bio Co. Ltd. references teach the commercial availability of the K35MONO anti-NC1 monoclonal antibody, which, absent evidence to the contrary, is identical to applicant's NC1 monoclonal antibody, Mono 12D, in view of applicant's specification at page 12.

Oftshun et al. teach an affinity membrane device in a columnar shape for the removal of deleterious solutes such as autoantibodies in the blood of Goodpasture's syndrome patients (see e.g. col. 19).

Sugihara et al. teach anti-NC1 autoantibodies in the blood of patients with Goodpasture's syndrome, an anti-glomerular basement membrane antibody-induced glomerulonephritis autoimmune disease.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have generated or purchased monoclonal antibodies, such as those available from Cosmo Bio Co. Ltd., for use in the removal methods of Yokoyama et al. in order to provide a potentially unlimited source of homogeneous reagent for use. It would have been further obvious to one of ordinary skill in the art at the time the instant invention was made to have used a device or a series of devices such as those taught in Oftshun et al. for the removal of NC1 antigen and anti-NC1 antibodies during dialysis as desired by Yokoyama et al., as modified in view of Cosmo Bio Co. Ltd. and applicant's specification, because Oftshun et al. teach their device for removal of deleterious solutes, such as autoantibodies, in the blood of patients, such as those having Goodpasture's syndrome, during dialysis and Sugihara et al. teach that anti-NC1 autoantibodies are pathologically found in the blood of patients with an anti-glomerular basement membrane antibody-induced glomerulonephritic disease such as Goodpasture's syndrome. One would have been motivated to remove both the anti-NC1 autoantibodies and

NC1 antigen during dialysis, particularly of Goodpasture's syndrome patients, in view of the direct suggestion in Yokoyama et al., as modified, to do so and would have expected the device of Oftshun et al., containing the appropriate immobilized ligands, to perform the expected function of affinity removal. Further, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art, e.g. to use the Mono 12D anti-NC1 monoclonal antibody (i.e. "K35MONO" in view of Cosmo Bio Co. Ltd. and applicant's specification at page 12) for antigen detection, cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Applicant's arguments filed 19 August 2009 have been fully considered but they are not deemed to be persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Moreover, the exercise of pairing the teachings of only some of the cited references, as argued by applicant, is equally unpersuasive. The question is not whether the combination of part or all of the references cited by the examiner was obvious to the applicant but whether the combination was obvious to a person of ordinary skill in the art.

Applicant urges that Yokoyama et al. do not teach detection of glomerulonephritis at an early stage. This is not found persuasive because, as set forth, the reference specifically teaches NC1 antigen and antibody detection for the determination of early stage glomerulonephritis or a risk therefor. One of ordinary skill in the art would understand that the early diagnosis taught by the reference would be at a stage before glomerular crescent formation because such is well known as an indicator of severe glomerular damage and disease (see e.g. Lan et al., Clin. Exp. Immunol. 110: 233, 1997).

Applicant urges that Sugihara et al. and Johansson et al. teach away from the invention as instantly claimed. This is not found persuasive because the teachings of the references relating to the presence of populations of noncollagenous domains of collagen (NC1) in glomerular basement membranes are not relied upon in the rejection of record and are not relevant to the methods of Yokoyama et al. involving enzyme-linked, or other label, immunosorbent immunoassays for the detection of circulating noncollagenous domain of collagen (NC1) antigen and antibodies specific for NC1 antigen in serum and urine biological samples from patients for the determination of early stage glomerulonephritis or a risk therefor. As set forth in the reasons of record, one would have been motivated to detect the antigen with available anti-NC1 monoclonal antibodies such as those commercially available from Cosmo Bio Co. Ltd. or as taught in Sugihara et al. or Johansson et al. motivated by the conventional substitution of monoclonal antibodies in an assay taught by Campbell.

Applicant urges that Oftshun et al. do not teach removal of anti-NC1 autoantibodies and NC1 antigen. This is not found persuasive for the reasons of record that one would have been motivated to remove both the anti-NC1 autoantibodies and NC1 antigen during dialysis,

particularly of Goodpasture's syndrome patients, in view of the direct suggestion in Yokoyama et al., as modified, to do so. Applicant's arguments of unexpected results were not found persuasive because, as set forth, one would have expected the device of Oftshun et al., containing the appropriate immobilized ligands taught by the combined teachings of the references set forth in the rejection of claims 18-20, to perform the expected function of affinity removal.

Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Lan et al. (Clin. Exp. Immunol. 110: 233, 1997) teach glomerular crescent formation as an indicator of severe glomerular damage and disease.

Ninomiya et al. (J. Cell Biol. 130: 1219, 1995) teach monoclonal antibodies specific for NC1 peptides and their use in various immunoassays.

Borza et al. (J. Biol. Chem. 276: 28532, 2001) elicited monoclonal antibodies to bovine glomerular basement membrane that bound to NC1 in ELISA and were also used in Western blotting reactions. The antibodies were used in affinity columns for purification of NC1 and were used in immunoprecipitation assays with protein G-sepharose.

Yokoyama et al. (Cell 34: 36, 2002) teach induction of glomerulonephritis by injection of the NC1 domain of type IV collagen. The submitted translation is incomplete, however, and it is not clear if immunofluorescent immunohistochemical assays were used to detect glomerulonephritis.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 11 a.m. to 7 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, SPE, can be contacted at (571) 272-0806.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/J. L. G./
James L. Grun, Ph.D.
Examiner, Art Unit 1641
December 7, 2009

/Shafiqul Haq/
Primary Examiner, Art Unit 1641